STN-Structure Search
10/25/06

10/567,472

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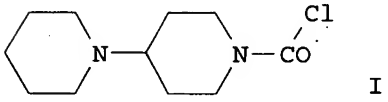
L7 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:817544 CAPLUS
DOCUMENT NUMBER: 145:230788
TITLE: Process for producing [1,4'-bipiperidine]-1'-carbonyl chloride or its hydrochloride salt
INVENTOR(S): Laitinen, Ilpo
PATENT ASSIGNEE(S): Fermion Oy, Finland
SOURCE: PCT Int. Appl., 12pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006084940	A1	20060817	WO 2006-FI32	20060206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-650535P P 20050208
OTHER SOURCE(S): CASREACT 145:230788
GI



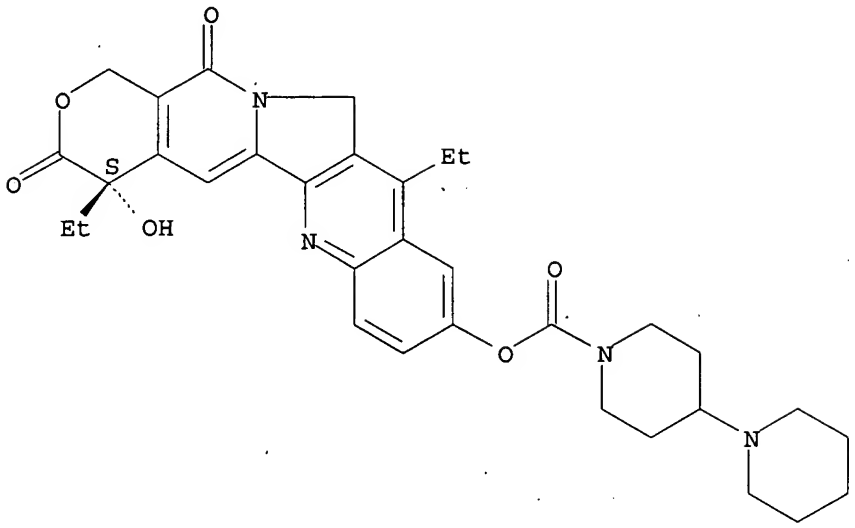
I

AB A process was disclosed for the preparation of [1,4']bipiperidinyl-1' -carbonyl chloride (I) or its hydrochloride salt using methylene chloride as a solvent in the reaction of 4-piperidinopiperidine with phosgene and removing the reaction solvent by using an addnl. distillation solvent to raise the distillation temperature I was further reacted with 7-ethyl-10-hydroxycamptothecin to form irinotecan hydrochloride, an antitumor alkaloid.

IT 97682-44-5P, Irinotecan
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; process for the preparation [1,4'-bipiperidine]-1'-carbonyl chloride or its hydrochloride salt an intermediate for the synthesis of the antitumor alkaloid irinotecan)

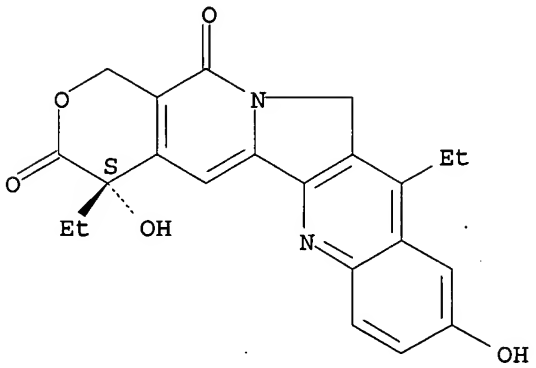
RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 86639-52-3, 7-Ethyl-10-hydroxycamptothecin
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation [1,4'-bipiperidine]-1'-carbonyl chloride or its hydrochloride salt an intermediate for the synthesis of the antitumor alkaloid irinotecan)
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:792754 CAPLUS
DOCUMENT NUMBER: 145:230787
TITLE: Process for the manufacturing of 7-ethyl-10-hydroxycamptothecin
INVENTOR(S): Laitinen, Ilpo
PATENT ASSIGNEE(S): Fermion Oy, Finland
SOURCE: PCT Int. Appl., 13pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

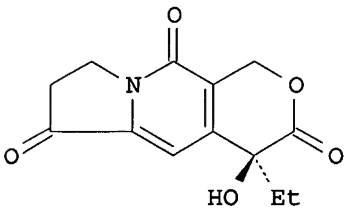
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006082279	A1	20060810	WO 2006-FI34	20060206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-650175P P 20050207
OTHER SOURCE(S): CASREACT 145:230787
GI



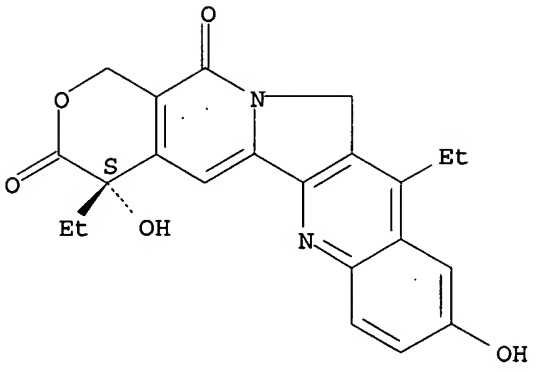
I

AB This invention disclosed a method for the preparation of 7-ethyl-10-hydroxycamptothecin from 4-ethyl-7,8-dihydro-4-hydroxy-1H-pyrano[3,4-f]indolizine-3,6,10(4H)-trione (I) and 1-(2-amino-5-hydroxyphenyl)propan-1-one using high reaction temperature and fast heating to that temperature

IT 86639-52-3P, 7-Ethyl-10-hydroxycamptothecin
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for manufacturing of 7-ethyl-10-hydroxycamptothecins)

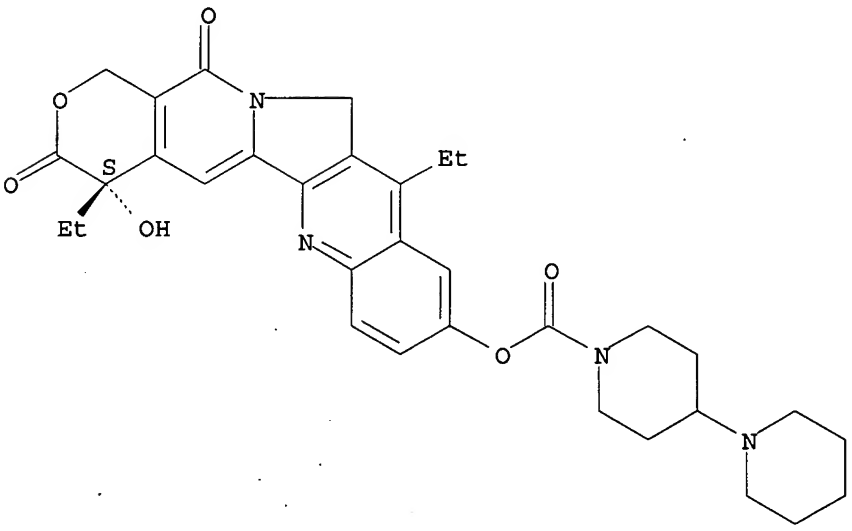
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 97682-44-5P, Irinotecan
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for manufacturing of 7-ethyl-10-hydroxycamptothecins)
RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

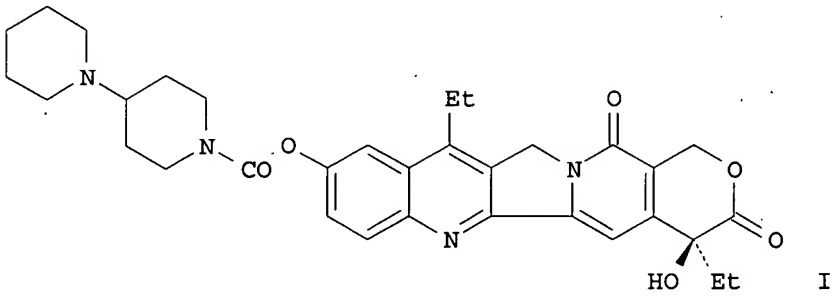
L7 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:151109 CAPLUS
DOCUMENT NUMBER: 144:233239
TITLE: An improved process for the preparation of irinotecan hydrochloride trihydrate
INVENTOR(S): Vishnukant, B.; Purohit, Prashant; Paparao, K.; Veereshapa
PATENT ASSIGNEE(S): Shilpa Medicare Limited, India
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016203	A1	20060216	WO 2004-IB2626	20040809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2004-IB2626 20040809
OTHER SOURCE(S): CASREACT 144:233239
GI



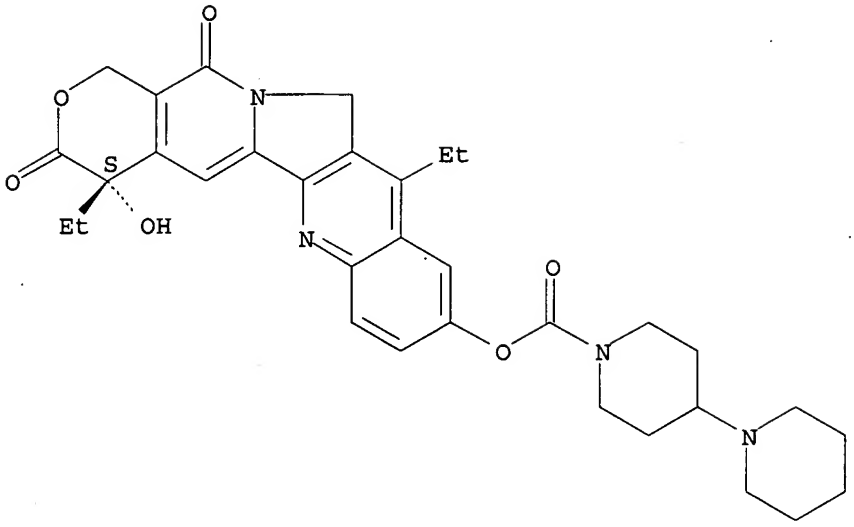
I

AB An improved process was disclosed for the preparation of irinotecan hydrochloride trihydrate of enhanced yield and purity and comprised reacting 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride with 7-ethyl-10-hydroxycamptothecin to obtain crude irinotecan (I) which was subsequently purified by solvent treatment, obtaining purified irinotecan which was converted into irinotecan hydrochloride trihydrate. This invention also relates to a report of 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride and a process for its preparation

IT 97682-44-5P, Irinotecan
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for preparation of irinotecan hydrochloride trihydrate)

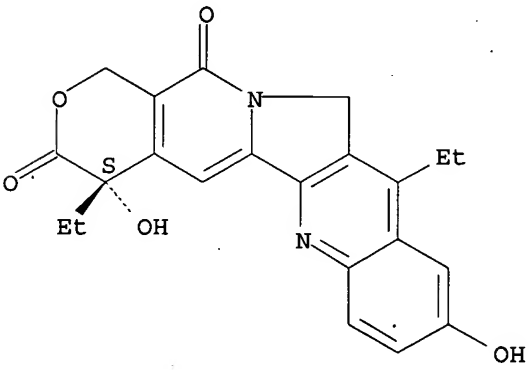
RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 86639-52-3P, 7-Ethyl-10-hydroxycamptothecin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for preparation of irinotecan hydrochloride trihydrate)
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1291999 CAPLUS
DOCUMENT NUMBER: 144:23039
TITLE: Process to prepare camptothecin derivatives and novel intermediate and compounds thereof
INVENTOR(S): Naidu, Ragina
PATENT ASSIGNEE(S): Phytogen Life Sciences Inc., Can.
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005272757	A1	20051208	US 2004-861097	20040604
WO 2005117881	A1	20051215	WO 2005-US19700	20050603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-861097 A 20040604

OTHER SOURCE(S): CASREACT 144:23039; MARPAT 144:23039

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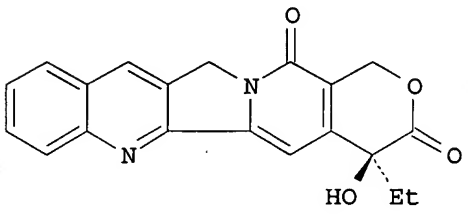


I

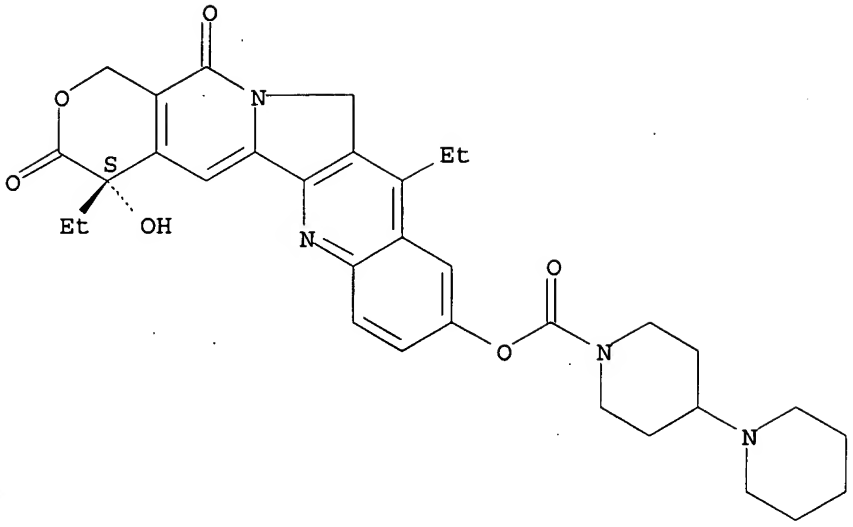
AB New processes are disclosed for the preparation of derivs. of camptothecin (I), such as, irinotecan and topotecan, as well as new intermediates and related compds.

IT 97682-44-5P, Irinotecan
RL: SPN (Synthetic preparation); PREP (Preparation)
(claimed compound; process for the preparation of camptothecin derivs.)

RN 97682-44-5 CAPLUS

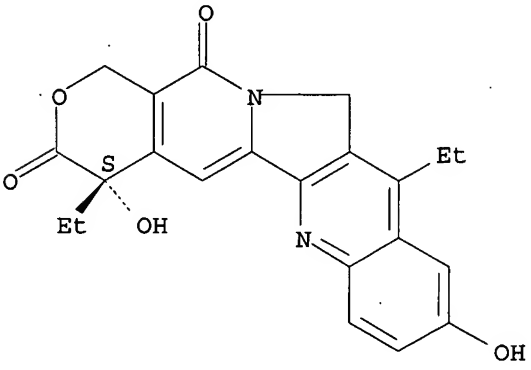
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 86639-52-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(claimed reactant; process for the preparation of camptothecin derivs.)
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1262080 CAPLUS
DOCUMENT NUMBER: 144:6956
TITLE: Process to prepare camptothecin derivatives
INVENTOR(S): Naidu, Ragina
PATENT ASSIGNEE(S): Phytogen Life Sciences Inc., Can.
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005267141	A1	20051201	US 2004-857170	20040528

WO 2005117879 A1 20051215 WO 2005-US18793 20050527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-857170 A 20040528
OTHER SOURCE(S): CASREACT 144:6956; MARPAT 144:6956

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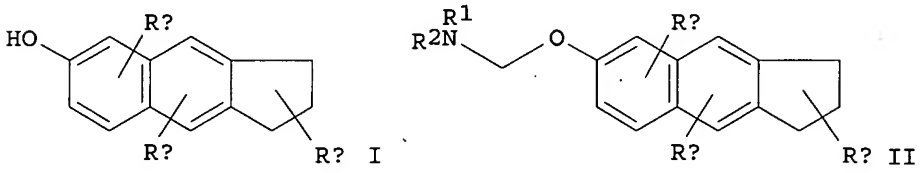


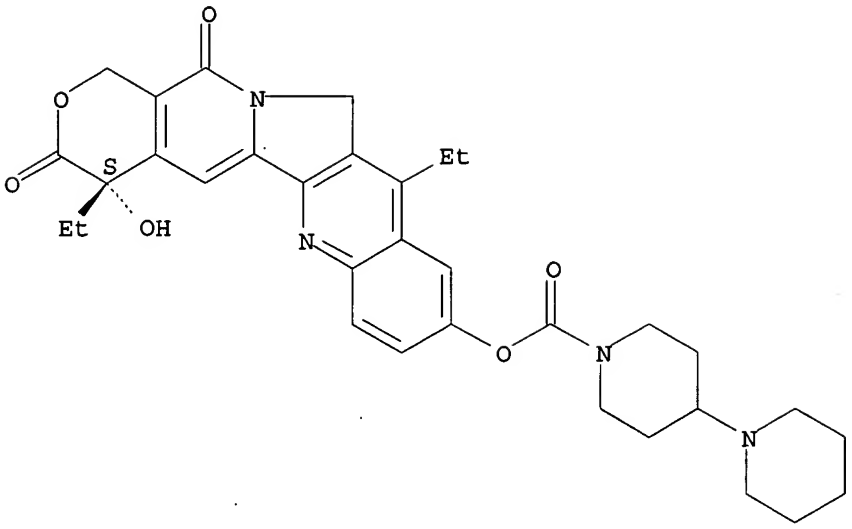
AB A process is provided for the preparation of camptothecin derivs., such as irinotecan, in a one-pot operation by treating the starting material I (wherein each of the ring atoms may be carbon, or any one, two, or three of the ring atoms may be N; Ra, Rb, Rc are the same or different and independently represent one or more optional non-hydrogen substituent on each of the rings A, B, C) with R1R2NH (R1, R2 are the same or different and independently represent organic groups) to give II. Thus, 4-piperidinopiperidine was treated with phosgene in CH2Cl2 containing N,N-diisopropylethylamine followed by addition of SN-38 to give 94% irinotecan after workup.

IT 97682-44-5P, Irinotecan
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process to prepare camptothecin derivs.)

RN 97682-44-5 CAPLUS

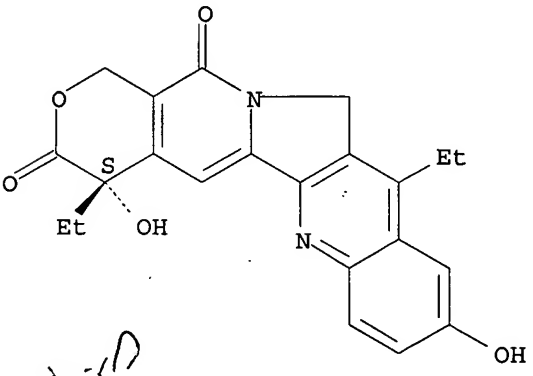
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 86639-52-3, Sn-38
RL: RCT (Reactant); RACT (Reactant or reagent)
(process to prepare camptothecin derivs.)
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



Inventor-SD

L7 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:182668 CAPLUS
DOCUMENT NUMBER: 142:280341
TITLE: Method of manufacturing of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (irinotecan base) by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride in the presence of 4-dimethylaminopyridine
INVENTOR(S): Dobrovolny, Petr
PATENT ASSIGNEE(S): Pliva-Lachema A. S., Czech Rep.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019223	A1	20050303	WO 2004-CZ50	20040824
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266752	A1	20050303	AU 2004-266752	20040824
EP 1664054	A1	20060607	EP 2004-762302	20040824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2006199961	A1	20060907	US 2006-567472	20060207
PRIORITY APPLN. INFO.:			CZ 2003-2305 A	20030826
			WO 2004-CZ50 W	20040824

OTHER SOURCE(S): CASREACT 142:280341

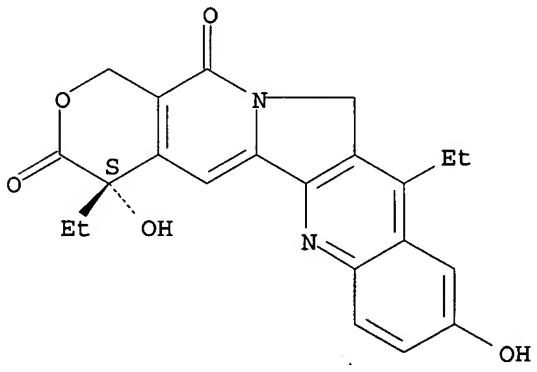
AB 7-Ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (i.e., irinotecan base) is prepared in high yield and selectivity by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride in a polar aprotic solvent in the presence of 4-dimethylaminopyridine.

IT 86639-52-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(method of manufacturing of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (irinotecan base) by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

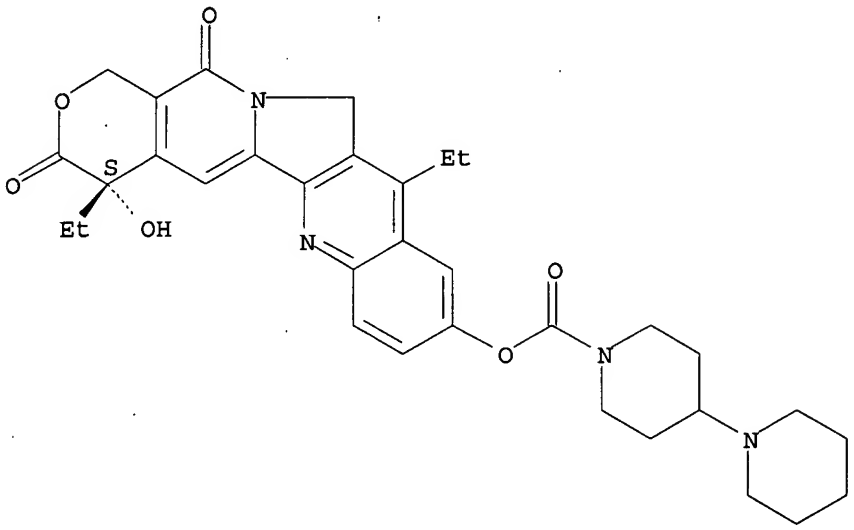


IT 97682-44-5P, Irinotecan
RL: SPN (Synthetic preparation); PREP (Preparation)
(method of manufacturing of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (irinotecan base) by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:658068 CAPLUS
DOCUMENT NUMBER: 137:201293
TITLE: Method of synthesizing camptothecin-relating compounds
INVENTOR(S): Ogawa, Takanori; Nishiyama, Hiroyuki; Uchida, Miyuki; Sawada, Seigo
PATENT ASSIGNEE(S): Kabushiki Kaisha Yakult Honsha, Japan
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066416	A1	20020829	WO 2002-JP1538	20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2437702	AA	20020829	CA 2002-2437702	20020221
EE 200300373	A	20031015	EE 2003-373	20020221
EP 1378505	A1	20040107	EP 2002-703874	20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1492851	A	20040428	CN 2002-805323	20020221
NZ 527615	A	20041224	NZ 2002-527615	20020221

BG 108031	A	20050430	BG 2003-108031		20030725
ZA 2003006223	A	20040603	ZA 2003-6223		20030812
NO 2003003579	A	20031010	NO 2003-3579		20030813
NZ 534374	A	20041224	NZ 2003-534374		20030814
US 2004106830	A1	20040603	US 2003-467987		20031218
US 7126000	B2	20061024			
PRIORITY APPLN. INFO.:			JP 2001-45430	A	20010221
			JP 2001-309322	A	20011005
			JP 2001-309332	A	20011005
			WO 2002-JP1538	W	20020221

OTHER SOURCE(S): CASREACT 137:201293; MARPAT 137:201293
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

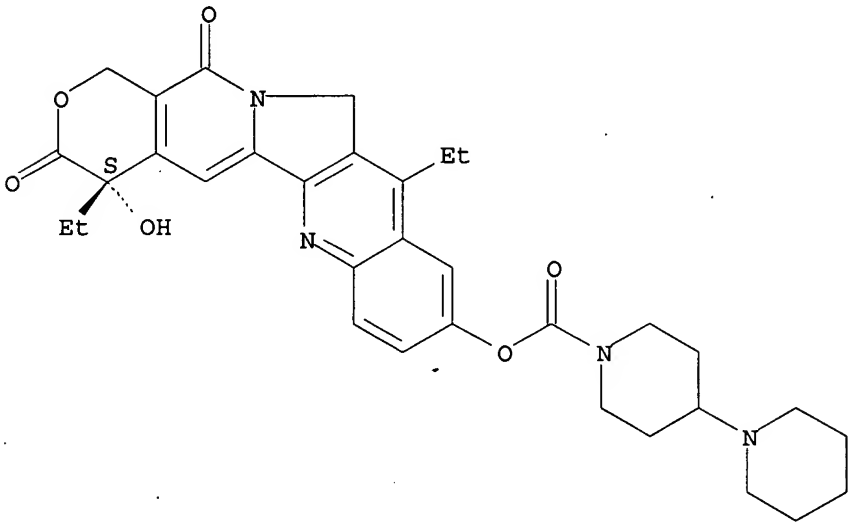
AB 2'-Amino-5'-hydroxypropiophenone (I) corresponding to the AB cycle moiety of the camptothecin (CPT) skeleton and a tricyclic ketone, namely (S)-4-ethyl-7,8-dihydro-4-hydroxy-1H-pyrano[3,4-f]indolizine-3,6,10(4H)-trione (II) corresponding to the CDE cycle moiety thereof can be efficiently produced and thus CPT and its derivs. can be stably supplied by a practically usable total synthesis to more efficiently provide camptothecin (CPT), which is a starting compound for irinotecan hydrochloride, namely 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin hydrochloride trihydrate, and various camptothecin derivs. Thus, benzylation of 2-nitro-5-hydroxybenzaldehyde by benzyl chloride in the presence of K2CO3 in DMF at 60° for 20 h gave 94% 5-benzyloxy-2-nitrobenzaldehyde which went addition reaction with vinylmagnesium bromide in THF at 3-10° for 1 h to give 84.0% 1-(5-benzyloxy-2-nitrophenyl)-2-propen-1-ol (VIII). Oxidation of VIII with MnO2 in CHCl3 at 25° for 15 h gave 91% 1-(5-benzyloxy-2-nitrophenyl)-1-oxo-2-propene which was hydrogenated over 10% Pd-C in EtOAc under H atmospheric for 13 h to give 81% I. K2OsO4.2H2O and (DHQD)2PYR were added to an aqueous solution of K3Fe(CN)6, K2CO3, and MeSO2NH2 and stirred at .apprx.5° for 1 h, followed by adding 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, and the resulting mixture was stirred at 5° for 20 h, treated with sodium sulfite, and stirred at 5° for 30 min for asym. dihydroxylation to give a diol (III) (95%) which was oxidized by iodine and K2CO3 in aqueous methanol at 40° for 48 h to give a lactone (IV; R = TMS) (88%). Iodination of IV (R = TMS) by iodine and CF3CO2Ag in CH2Cl2 at room temperature for 16.5 h gave IV (R = iodo) (97%) which underwent carbonylation by CO in the presence of Pd(OAc)2 and K2CO3 in 1-propanol at 60° for 18 to give an ester IV (R = n-PrO2C) (70%). Demethylation of IV (R = n-PrO2C) by treatment with Me3SiCl and NaI in MeCN at room temperature for 3 h gave a keto lactone, namely 4-ethyl-3,4,7,8-tetrahydro-4-hydroxy-3,8-dioxo-1H-pyrano[3,4-c]pyridine-6-carboxylic acid Pr ester (V) (95%) which was cyclocondensed with tert-Bu acrylate in the presence of K2CO3 in DMSO at 50° for 20 min to give a tricyclic compound (VI) (77%). VI was heated with a mixture of CF3CO2H and PhMe at 110° for 100 min to give 77% II which was cyclocondensed with I in a 1:1 mixture of AcOH and toluene in the presence of p-toluenesulfonic acid monohydrate at 100° for 18 h to give SN-38 (VII; R1= H). VII (R1= H) was converted into irinotecan hydrochloride, VII.HCl (R1 = Q).

IT 97682-44-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of camptothecin-relating compds. such as irinotecan hydrochloride and intermediates thereof)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

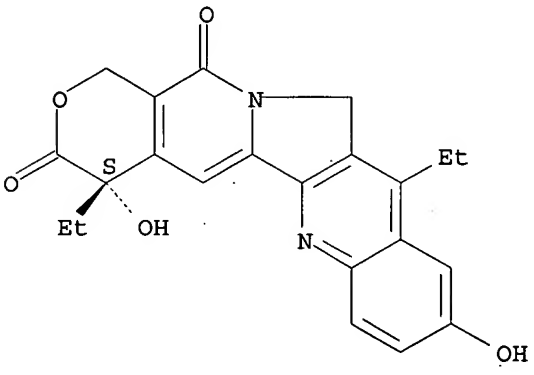


IT 86639-52-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of camptothecin-relating compds. such as irinotecan hydrochloride and intermediates thereof)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:713182 CAPLUS
DOCUMENT NUMBER: 135:262261
TITLE: Preparation and antitumor activity of polyglutamic acid-camptothecin conjugates
INVENTOR(S): Bhatt, Rama; De Vries, Peter; Klein, J. Peter; Lewis, Robert A.; Singer, Jack W.; Tulinsky, John

PATENT ASSIGNEE(S): Cell Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001070275	A2	20010927	WO 2001-US8553		20010319
WO 2001070275	A3	20020103			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2402643	AA	20010927	CA 2001-2402643		20010319
AU 2001047513	A5	20011003	AU 2001-47513		20010319
EP 1267939	A2	20030102	EP 2001-920466		20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003527443	T2	20030916	JP 2001-568471		20010319
SI 21172	C	20031031	SI 2001-20021		20010319
BR 2001009272	A	20040629	BR 2001-9272		20010319
NO 2002004421	A	20021115	NO 2002-4421		20020916
ZA 2002007423	A	20031217	ZA 2002-7423		20020916
PRIORITY APPLN. INFO.:			US 2000-190429P	P	20000317
			WO 2001-US8553	W	20010319

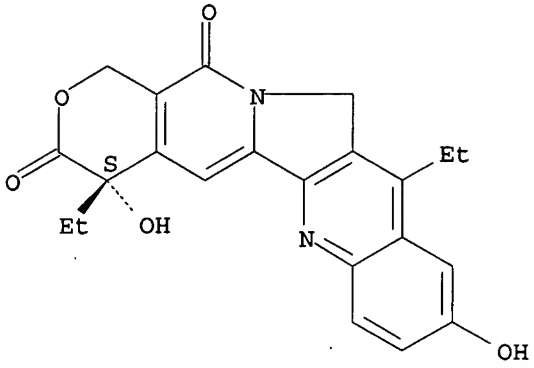
OTHER SOURCE(S): MARPAT 135:262261

AB Methods for the preparation of polyglutamic acid-therapeutic agent conjugates are disclosed. The compds. show antitumor activity. Thus, 20(S)-camptothecin was allowed to react with N-(tert-butoxycarbonyl)glycine in DMF solution in the presence of 4-dimethylaminopyridine followed by the addition of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The product, 20-O-(N-(tert-butoxycarbonyl)glycyl)camptothecin, was deprotected with CF3CO2H to give 20-O-(glycyl)camptothecintrifluoroacetic acid salt which was then treated with poly-(L-glutamic acid). The conjugate, polyglutamate-glycine-camptothecin showed high antitumor activity.

IT 86639-52-3, SN 38
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of polyglutamic acid-camptothecin conjugates)

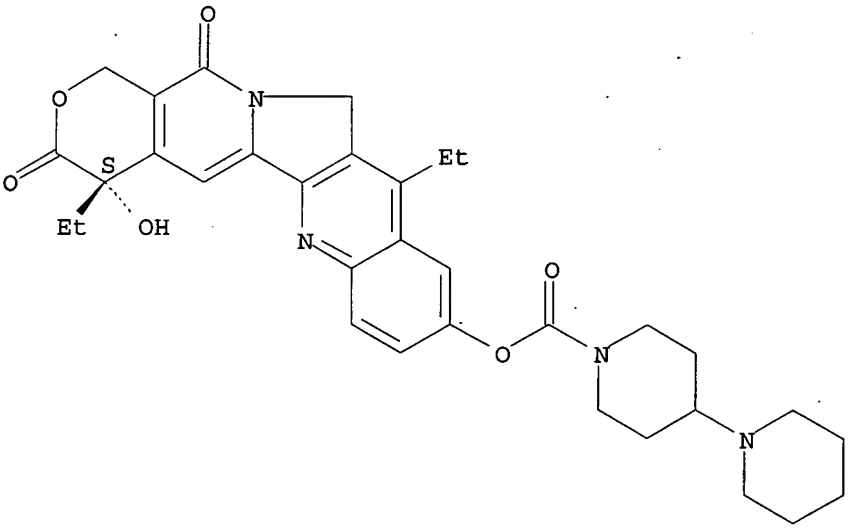
RN 86639-52-3 CAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 97682-44-5DP, Irinotecan, polyglutamic acid conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of polyglutamic acid-camptothecin conjugates)
RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:701089 CAPLUS
DOCUMENT NUMBER: 136:369880
TITLE: Improved method for the synthesis of Irinotecan
AUTHOR(S): Li, Yuyan; You, Qidong; Li, Zhiyu; Wang, Hua
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2001), 11(4), 238-240
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

OTHER SOURCE(S): CASREACT 136:369880

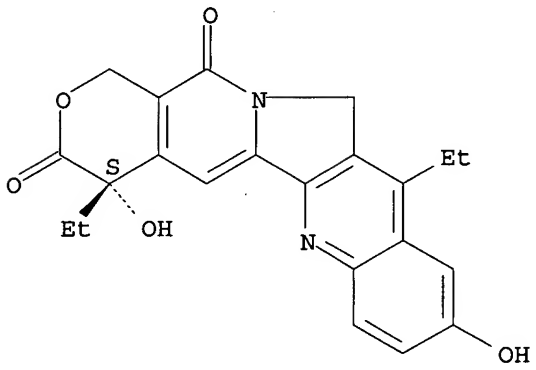
AB Irinotecan was synthesized by alkylation camptothecin with propionaldehyde in water-glacial acetic acid in the presence of FeSO4 7H2O and H2SO4, oxidization with H2O2 at 80° for 3 h, rearrangement in dioxane-acetonitrile-water (25:50:8, volume/volume) in the presence of H2SO4 under illumination for 15 min to obtain 7-ethyl-10-hydroxycamptothecin; further acylation with 4-(1-piperidyl)piperidine-1-carbonylchloride, giving the product with overall yield 21%.

IT 86639-52-3P, 7-Ethyl-10-hydroxycamptothecin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved method for the synthesis of Irinotecan)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

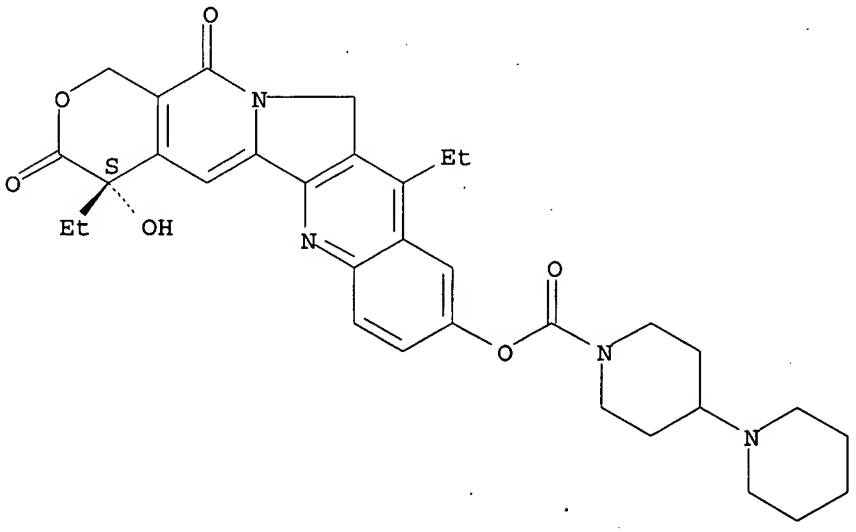


IT 97682-44-5P, Irinotecan
RL: SPN (Synthetic preparation); PREP (Preparation)
(improved method for the synthesis of Irinotecan)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

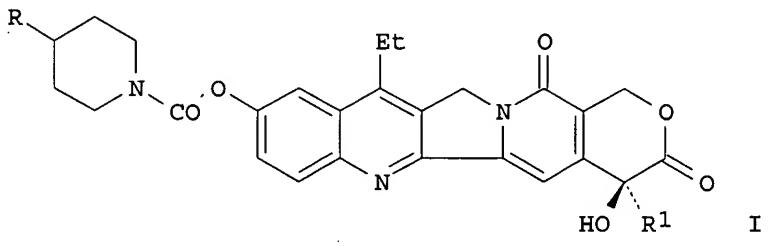


L7 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:48724 CAPLUS
DOCUMENT NUMBER: 130:125257
TITLE: Synthesis of and intermediates for camptothecins
INVENTOR(S): Curran, Dennis P.; Bom, David
PATENT ASSIGNEE(S): University of Pittsburgh, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901456	A1	19990114	WO 1998-US13941	19980702
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6252079	B1	20010626	US 1997-886093	19970702
AU 9884761	A1	19990125	AU 1998-84761	19980702

PRIORITY APPLN. INFO.:	US 1997-886093	A	19970702
	US 1993-85190	B2	19930630
	US 1995-436799	B2	19950508
	WO 1998-US13941	W	19980702

OTHER SOURCE(S): CASREACT 130:125257; MARPAT 130:125257
GI



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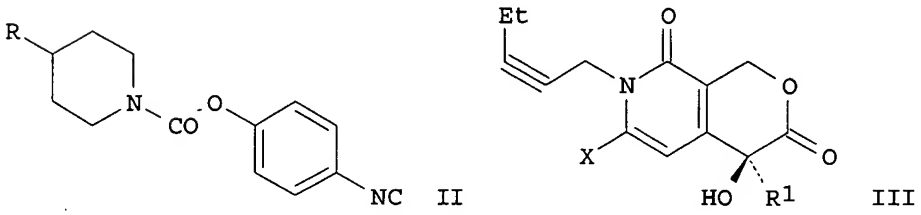


II III

AB Camptothecin analogs, such as I [R = H, alkoxy, N containing heterocyclyl, such as piperidinyl; R1 = allyl, propargyl, benzyl, alkyl], were prepared via a novel [4 + 1] radical annulation of the corresponding isonitriles II with pyridinones III [X = Br, iodo] for use as topoisomerase inhibitors. Thus, (+)-irinotecan I [R = piperidinyl, R1 = Et] was prepd in 31% yield by cyclization of isonitrile II [R = piperidinyl] with pyridinone III [R1 = Et, X = iodo] in the presence of hexadimethylditin in benzene. The prepared compds were tested for topoisomerase I inhibiting activity and

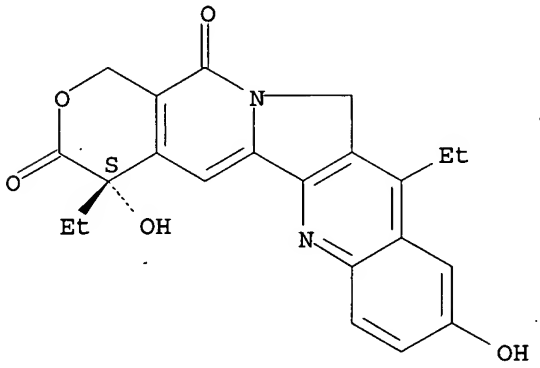
cytotoxic activity against HL-60 human promyelocytic leukemic cells and against 833K human teratocarcinoma cells.

IT 86639-52-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of camptothecins via radical cyclization for use as topoisomerase inhibitors)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

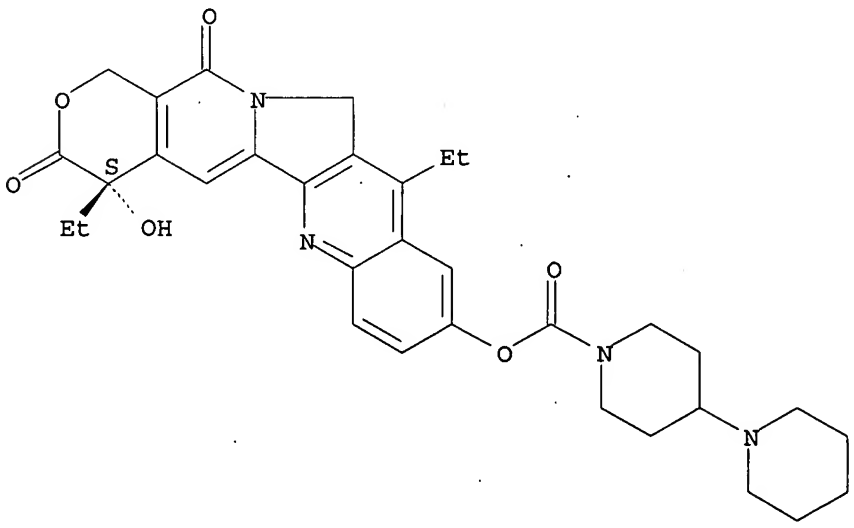


IT 97682-44-5P, (+)-Irinotecan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of camptothecins via radical cyclization for use as topoisomerase inhibitors)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:701701 CAPLUS
DOCUMENT NUMBER: 125:329101
TITLE: Novel intermediates and process for the manufacture of camptothecin derivatives (CPT-11) and related compounds
INVENTOR(S): Henegar, Kevin E.; Sih, John C.
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

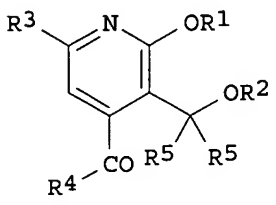
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631513	A1	19961010	WO 1996-US4163	19960401
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
TW 438775	B	20010607	TW 1996-85103680	19960327
IL 117684	A1	20020210	IL 1996-117684	19960327
CA 2214793	AA	19961010	CA 1996-2214793	19960401
AU 9655278	A1	19961023	AU 1996-55278	19960401
AU 717179	B2	20000316		
EP 835257	A1	19980415	EP 1996-912468	19960401
EP 835257	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1181083	A	19980506	CN 1996-193138	19960401
CN 1100058	B	20030129		
JP 11503156	T2	19990323	JP 1996-530356	19960401
RU 2164917	C2	20010410	RU 1997-118673	19960401
AT 224899	E	20021015	AT 1996-912468	19960401
PT 835257	T	20030131	PT 1996-912468	19960401
ES 2183943	T3	20030401	ES 1996-912468	19960401
PL 186446	B1	20040130	PL 1996-322651	19960401
PL 186564	B1	20040130	PL 1996-355318	19960401
ZA 9602747	A	19980406	ZA 1996-2747	19960404
US 6121451	A	20000919	US 1997-230245	19971002
NO 9704608	A	19971208	NO 1997-4608	19971006
NO 320482	B1	20051212		
HK 1009448	A1	20030606	HK 1998-110439	19980904
US 6235907	B1	20010522	US 2000-511006	20000222
US 6444820	B1	20020903	US 2000-687227	20001013
CN 1434044	A	20030806	CN 2003-103097	20030123
CN 1434043	A	20030806	CN 2003-103098	20030123
CN 1434046	A	20030806	CN 2003-103099	20030123
CN 1434037	A	20030806	CN 2003-103100	20030123
HK 1055119	A1	20060922	HK 2003-107420	20031015
NO 2005000408	A	19971208	NO 2005-408	20050125

PRIORITY APPLN. INFO.:		
US 1995-419643	A2	19950407
WO 1996-US4163	W	19960401
US 1997-230245	A3	19971002

US 2000-511006 A3 20000222

OTHER SOURCE(S): MARPAT 125:329101

GI



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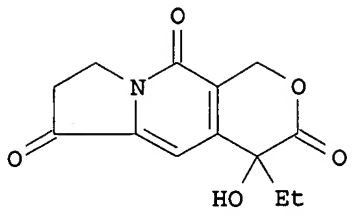


II

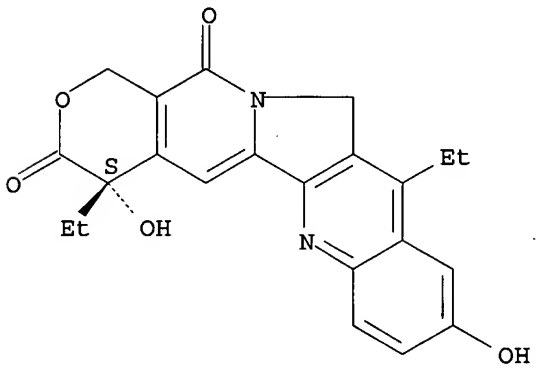
AB Preparation of novel intermediates, e.g. pyridines I (R1 = alkyl, cycloalkyl, alkenyl, aryl; R2 = alkyl, cycloalkyl, alkenyl, aryl; R3 = Cl, alkyl-, cycloalkyl-, alkenyl-, aryl-ester; R4 = alkyl, cycloalkyl, aryl; R4 = independently H, alkyl, aryl), and procedures for the synthesis of camptothecin derivs., e.g. irinotecan, and related compds., e.g. mappicine, were disclosed. Thus, I [R1 = Me, R2 = benzyl, R3 = CO2(CH2)CH3, R4 = Et, R5 = H] was prepared in several steps starting from citrazinic acid and was further converted to known camptothecin intermediate (II) via another series of steps.

IT 86639-52-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel intermediates and process for the manufacture of camptothecin derivs. and related compds.)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

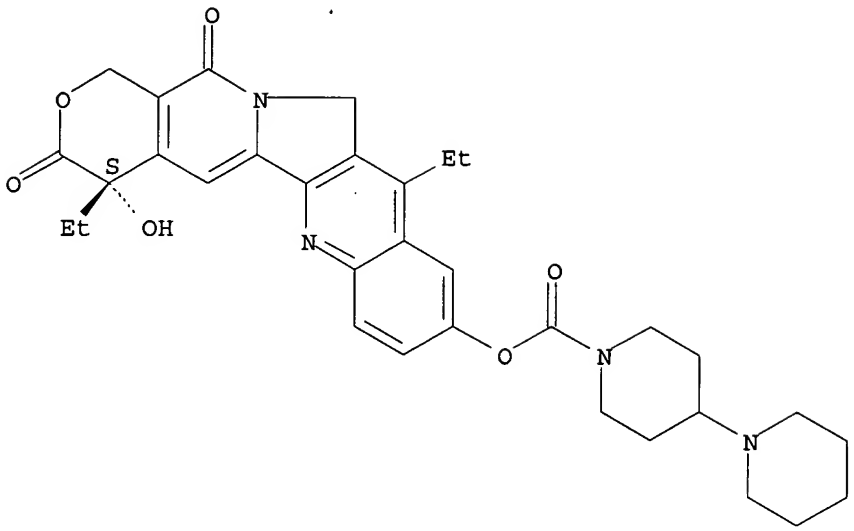


IT 97682-44-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(novel intermediates and process for the manufacture of camptothecin derivs. and related compds.)

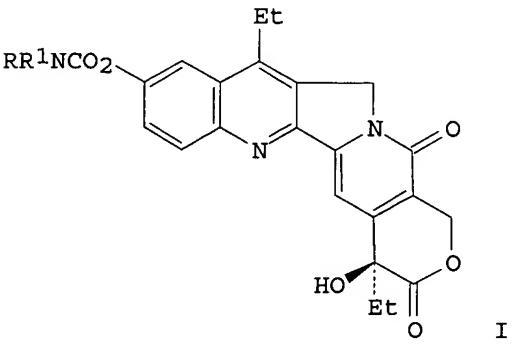
RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:583643 CAPLUS
DOCUMENT NUMBER: 115:183643
TITLE: Synthesis and antitumor activity of 20(S)-camptothecin derivatives: carbamate-linked, water-soluble derivatives of 7-ethyl-10-hydroxycamptothecin
AUTHOR(S): Sawada, Seigo; Okajima, Satoru; Aiyama, Ritsuo; Nokata, Kenichiro; Furuta, Tomio; Yokokura, Teruo; Sugino, Eiichi; Yamaguchi, Kentaro; Miyasaka, Tadashi
CORPORATE SOURCE: Yakult Inst. Microbiol. Res., Kunitachi, 186, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(6), 1446-54
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Novel 36 derivs. bonding the phenolic hydroxyl group of 7-ethyl-10-hydroxycamptothecin with diamines through a monocarbamate linkage, e.g. I (R = lower alkyl, R1 = Me2NCH2CH2, Et2NCH2CH2, RR1N = substituted piperazino, aminopiperidino) were synthesized and their antitumor activity was evaluated in vivo. The derivs. were soluble in water as their HCl salts with the E lactone ring intact and exhibited significant antitumor activity. I (RR1N = 4-piperidinopiperidino) showed excellent activity against L1210 leukemia and other murine tumors. The

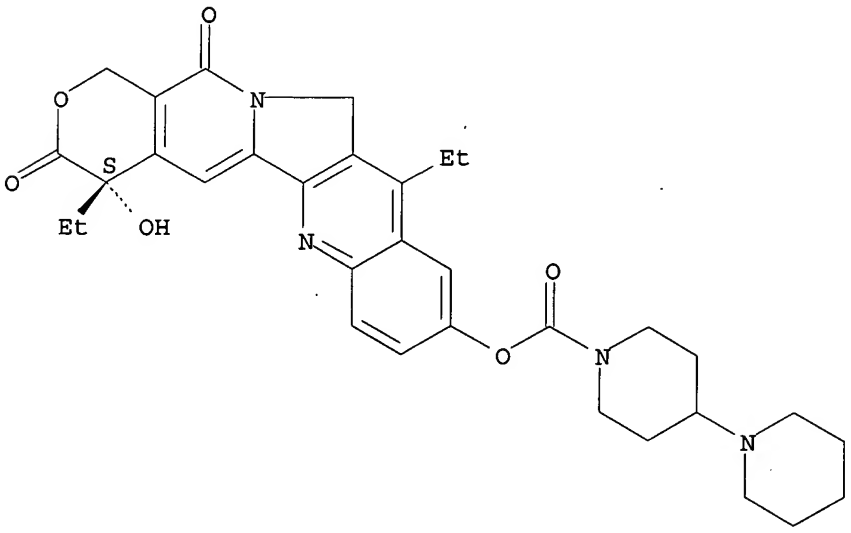
structure of its hydrochloride trihydrate was determined by spectroscopic and crystallog. methods.

IT 97682-44-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

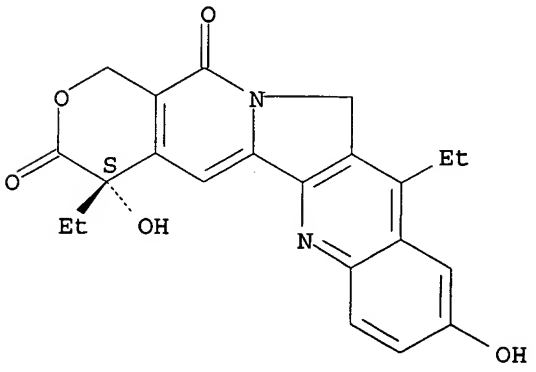


IT 86639-52-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with phosgene and chlorocarbonyldiamines)

RN 86639-52-3 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

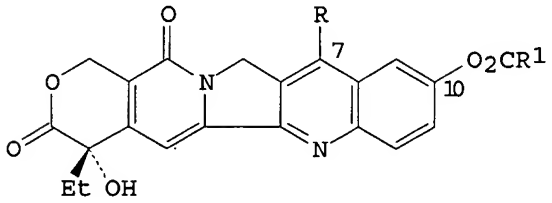


L7 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:488119 CAPLUS

DOCUMENT NUMBER: 103:88119
TITLE: Camptothecin derivatives
PATENT ASSIGNEE(S): Yakult Honsha Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 60019790	A2	19850131	JP 1983-126946		19830714
JP 03004077	B4	19910122			
US 4604463	A	19860805	US 1984-627980		19840705
CA 1235415	A1	19880419	CA 1984-458228		19840705
EP 137145	A1	19850417	EP 1984-108257		19840713
EP 137145	B1	19880427			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
AT 33839	E	19880515	AT 1984-108257		19840713
PRIORITY APPLN. INFO.:			JP 1983-126946	A	19830714
			EP 1984-108257	A	19840713

OTHER SOURCE(S): CASREACT 103:88119; MARPAT 103:88119
GI



I

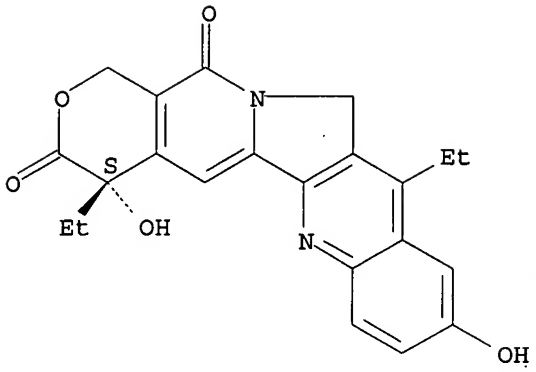
AB Twenty camptothecin derivs. I [R = H, alkyl; R1 = Cl, NR2R3 (R2, R3 = H, (un)substituted alkyl; R2 and R3 may form a heterocyclic)] were prepared as anticarbinogens or their intermediates (no data). Thus, 400 μL COCl2 dimer was decomposed in the presence of active C and the resulting COCl2 fed to a mixture of 500 mg 7-ethyl-10-hydroxycamptothecin and 2 mL Et3N in dioxane 0.5 h at room temperature to give 97.4% I (R = Et, R1 = Cl).

IT 86639-52-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(chloroformylation of)

RN 86639-52-3 CAPLUS

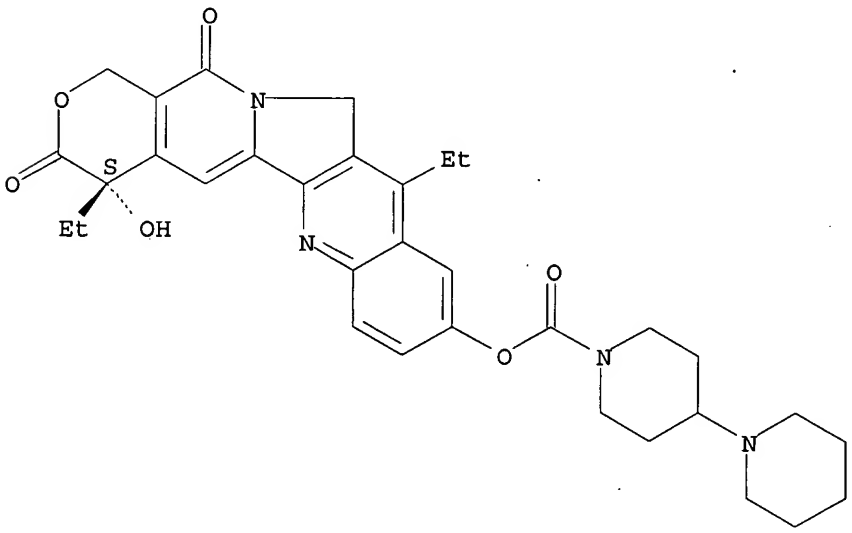
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4,9-dihydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 97682-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



=> d his

(FILE 'HOME' ENTERED AT 10:04:49 ON 25 OCT 2006)

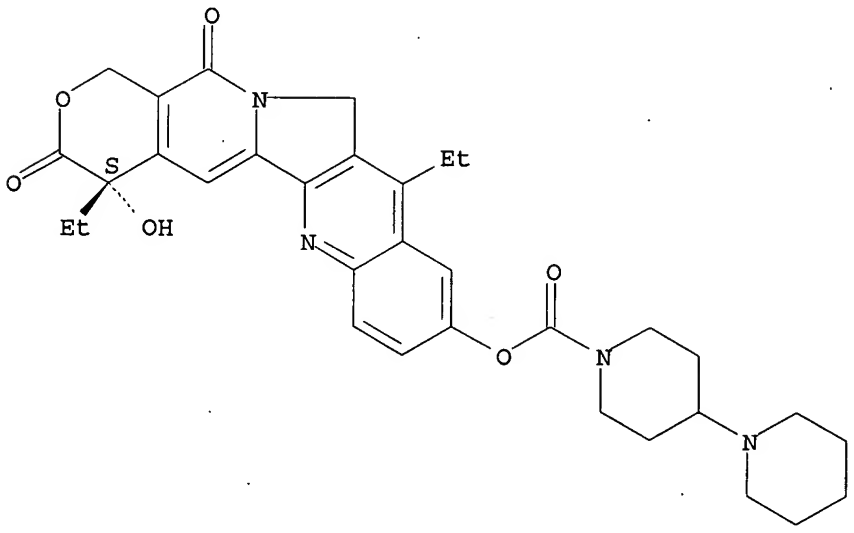
FILE 'REGISTRY' ENTERED AT 10:05:08 ON 25 OCT 2006
L1 1 S IRINOTECAN/CN
L2 STRUCTURE UPLOADED
L3 0 S L2
L4 40 S L2 FULL

FILE 'CAPLUS' ENTERED AT 10:07:01 ON 25 OCT 2006
L5 33 S L1/PREP
L6 65 S L4/RCT
L7 13 S L5 AND L6

=> d l1
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 97682-44-5 REGISTRY
ED Entered STN: 18 Aug 1985
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline, [1,4'-bipiperidine]-1'-carboxylic acid deriv.
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, (S)-
OTHER NAMES:
CN (+)-Irinotecan
CN Irinotecan
CN Irinotecan lactone
FS STEREOSEARCH
MF C33 H38 N4 O6
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1783 REFERENCES IN FILE CA (1907 TO DATE)
46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1795 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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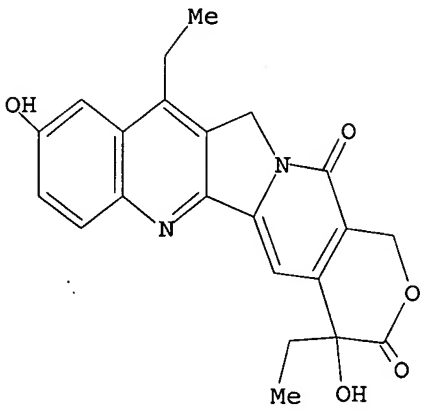
L2 HAS NO ANSWERS
L2 STR



Structure attributes must be viewed using STN Express query preparation.

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L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:182668 CAPLUS
DOCUMENT NUMBER: 142:280341
TITLE: Method of manufacturing of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (irinotecan base) by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride in the presence of 4-dimethylaminopyridine
INVENTOR(S): Dobrovolny, Petr
PATENT ASSIGNEE(S): Pliva-Lachema A. S., Czech Rep.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005019223	A1	20050303	WO 2004-CZ50		20040824
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004266752	A1	20050303	AU 2004-266752		20040824
EP 1664054	A1	20060607	EP 2004-762302		20040824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR					
US 2006199961	A1	20060907	US 2006-567472		20060207
PRIORITY APPLN. INFO.:			CZ 2003-2305	A	20030826
			WO 2004-CZ50	W	20040824

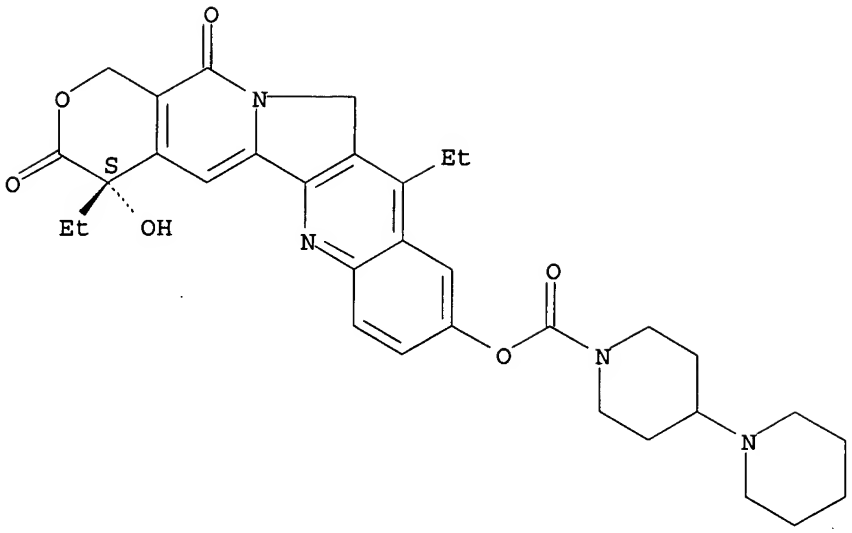
OTHER SOURCE(S): CASREACT 142:280341

AB 7-Ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (i.e., irinotecan base) is prepared in high yield and selectivity by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride in a polar aprotic solvent in the presence of 4-dimethylaminopyridine.

IT 97682-44-5P, Irinotecan
RL: SPN (Synthetic preparation); PREP (Preparation)
(method of manufacturing of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (irinotecan base) by the esterification of 7-ethyl-10-hydroxycamptothecin with 1-chlorocarbonyl-4-piperidinopiperidine hydrochloride)

RN 97682-44-5 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:713182 CAPLUS
DOCUMENT NUMBER: 135:262261
TITLE: Preparation and antitumor activity of polyglutamic acid-camptothecin conjugates
INVENTOR(S): Bhatt, Rama; De Vries, Peter; Klein, J. Peter; Lewis, Robert A.; Singer, Jack W.; Tulinsky, John
PATENT ASSIGNEE(S): Cell Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070275	A2	20010927	WO 2001-US8553	20010319
WO 2001070275	A3	20020103		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402643	AA	20010927	CA 2001-2402643	20010319
AU 2001047513	A5	20011003	AU 2001-47513	20010319
EP 1267939	A2	20030102	EP 2001-920466	20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527443	T2	20030916	JP 2001-568471	20010319
SI 21172	C	20031031	SI 2001-20021	20010319
BR 2001009272	A	20040629	BR 2001-9272	20010319
NO 2002004421	A	20021115	NO 2002-4421	20020916
ZA 2002007423	A	20031217	ZA 2002-7423	20020916

PRIORITY APPLN. INFO.: US 2000-190429P P 20000317
WO 2001-US8553 W 20010319

OTHER SOURCE(S): MARPAT 135:262261

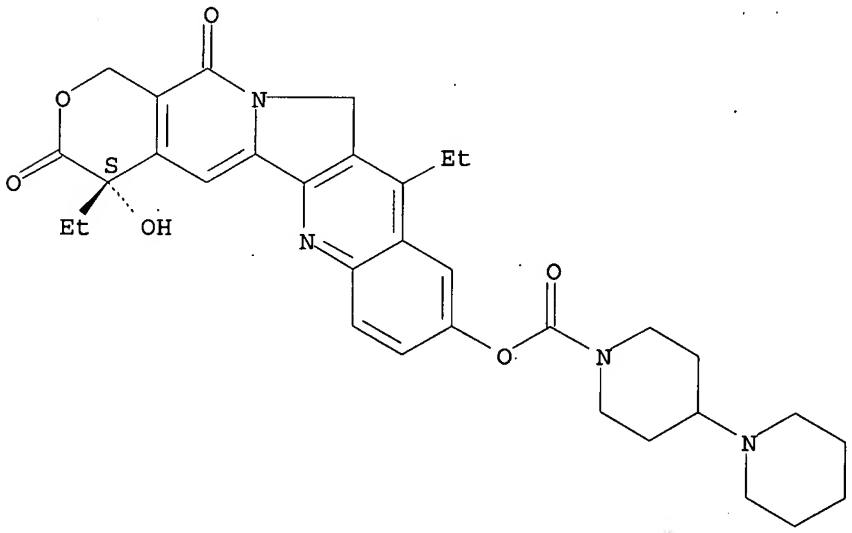
AB Methods for the preparation of polyglutamic acid-therapeutic agent conjugates are disclosed. The compds. show antitumor activity. Thus, 20(S)-camptothecin was allowed to react with N-(tert-butoxycarbonyl)glycine in DMF solution in the presence of 4-dimethylaminopyridine followed by the addition of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The product, 20-O-(N-(tert-butoxycarbonyl)glycyl)camptothecin, was deprotected with CF3CO2H to give 20-O-(glycyl)camptothecintrifluoroacetic acid salt which was then treated with poly-(L-glutamic acid). The conjugate, polyglutamate-glycine-camptothecin showed high antitumor activity.

IT 97682-44-5DP, Irinotecan, polyglutamic acid conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of polyglutamic acid-camptothecin conjugates)

RN 97682-44-5 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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(FILE 'HOME' ENTERED AT 10:23:44 ON 25 OCT 2006)

FILE 'REGISTRY' ENTERED AT 10:23:56 ON 25 OCT 2006
L1 1 S IRINOTECAN/CN

FILE 'CAPLUS' ENTERED AT 10:24:31 ON 25 OCT 2006
L2 33 S L1/PREP
L3 2439 S 4-DIMETHYLAMINOPYRIDINE
L4 2 S L2 AND L3

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